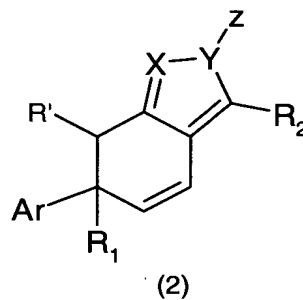
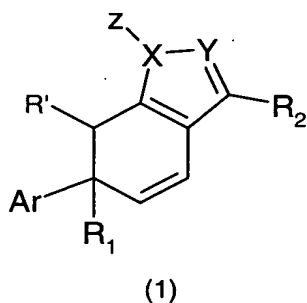


What is claimed is:

1. A compound of formula (1) or formula (2)



wherein:

X and Y independently are N or CH wherein at least one of X and Y is N;

Ar is:

phenyl optionally substituted with one or more substituents selected from the group consisting of: halogen, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, thio(C₁-C₄)alkyl, NO₂, NH(C₁-C₄)alkyl and N((C₁-C₄)alkyl)₂ wherein said alkyl may optionally form a 4 to 6 membered ring together with the heteroatom to which it is attached and an ortho carbon of the phenyl wherein said 4 to 6 membered ring may contain a second hetero atom selected from the group consisting of O, S and N, or

5 or 6 membered aromatic heterocycle containing one or two hetero atoms selected from the group consisting of O, N and S, and optionally substituted with one or more halogen, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, thio(C₁-C₄)alkyl, NH(C₁-C₄)alkyl, N((C₁-C₄)alkyl)₂ wherein said alkyl may optionally form a 4 to 6 membered ring together with the heteroatom to which it is attached and an ortho carbon of said heterocycle wherein said 4 to 6 membered ring may optionally contain a second hetero atom selected from the group consisting of O, S and N,

Z is H, 4-aminophenyl, SO₂R₃ or COR₃ wherein R₃ is (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl,

Ar as defined above, (C₂-C₆)alkenyl or (C₂-C₆)alkynyl;

R₁ is H, (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl or Ar as defined above;

R' is H or (C₁-C₄)alkyl; and

when Z is H, R₂ is a selected from the group consisting of:

cyano,

C(O)-ORa₁ wherein Ra₁ is methyl, ethyl or isopropyl,

C(O)-NHRa₂ wherein Ra₂ is cyclopropyl,

C(O)-N(Ra₂'), wherein N(Ra₂') is aziridinyl or azetidiny, optionally substituted
5 with (C₁-C₄)alkyl or Ar as defined above,

C(O)-N(Ra₃)-ORa₃ wherein each Ra₃ may be identical or different and each
Ra₃ is independently selected from the group consisting of methyl,
ethyl or cyclopropyl,

C(O)Ra₄ wherein Ra₄ is Ar as defined above or (C₃-C₅)cycloalkyl optionally
10 substituted with (C₁-C₄)alkyl or Ar as defined above,

C(Ra₄)=N-Rb wherein:

Ra₄ is H, Ar as defined above, or (C₃-C₅)cycloalkyl optionally
substituted with (C₁-C₄)alkyl or Ar as defined above, and

Rb is (C₁-C₂)alkyl, (C₃-C₅)cycloalkyl, hydroxyl, (C₁-C₄)alkoxy,
15 (C₂-C₄)alkenyloxy, or (C₁-C₄)alkylenoxy wherein said
(C₁-C₄)alkylenoxy optionally may be substituted with halogen or a
group selected from the group consisting of carboxyl, (CH₂)_nAr
wherein n is 0 or 1 and Ar is as defined above, (C₁-C₄)alkoxy, NH₂,
NH(C₁-C₄)alkyl, and N((C₁-C₄)alkyl)₂ wherein said alkyls together
20 with the heteroatom to which they are attached may optionally form
a 3 to 6 membered ring which may optionally contain a second
hetero atom selected from the group consisting of O, S and N,

NH-C(O)Ra₄ wherein Ra₄ is H, Ar as defined above, or (C₃-C₅)cycloalkyl
optionally substituted with (C₁-C₄)alkyl or Ar as defined above,

25 NHRa₄ wherein Ra₄ is H, Ar as defined above, or (C₃-C₅)cycloalkyl optionally
substituted with (C₁-C₄)alkyl or Ar as defined above,

phenyl, and

5 to 6 membered aromatic heterocycle containing 1 to 3 hetero atoms selected
from the group consisting of O, N and S; and

30 when Z is SO₂R₃ or COR₃, R₂ is carboxyl, NH₂, NH(C₁-C₄)alkyl, N((C₁-C₄)alkyl)₂ or
(C₃-C₅)cycloalkylamino; or

a stereoisomeric form of the compound of formula (1) or formula (2), or mixtures of
the stereoisomeric forms thereof in any ratio; or

a pharmaceutically acceptable salt of the compound of formula (1) or formula (2).

2. The compound according to claim 1 wherein Ar is phenyl, 4-fluorophenyl or 4-methoxyphenyl.

3. The compound according to claim 2 wherein R₁ is H, (C₁-C₄)alkyl, phenyl or substituted phenyl.

4. The compound according to claim 3 wherein X and Y is each N and Z is H.

5. The compound according to claim 4 wherein R₂ is C(O)-ORa₁ and wherein Ra₁ is (C₁-C₄)alkyl.

6. The compound according to claim 5 selected from the group consisting of:

ethyl 6,6-diphenyl-6,7-dihydro-2H-indazole-3-carboxylate,
isopropyl 6,6-diphenyl-6,7-dihydro-2H-indazole-3-carboxylate,
methyl 6,6-diphenyl-6,7-dihydro-2H-indazole-3-carboxylate,
ethyl 6-(R,S)-6-methyl-6-phenyl-6,7-dihydro-1H-indazole-3-carboxylate,
ethyl 6-(+)-6-methyl-6-phenyl-6,7-dihydro-1H-indazole-3-carboxylate,
ethyl 6-(R,S)-6-phenyl-6,7-dihydro-2H-indazole-3-carboxylate,
ethyl 6-(R)-6-phenyl-6,7-dihydro-2H-indazole-3-carboxylate,
ethyl 6-(S)-6-phenyl-6,7-dihydro-2H-indazole-3-carboxylate,
ethyl 6,6-bis(4-methoxyphenyl)-6,7-dihydro-1H-indazole-3-carboxylate,
ethyl 6-(R,S)-6-(3,4-dimethoxyphenyl)-6-phenyl-6,7-dihydro-1H-indazole-3-carboxylate,
ethyl 6-(R,S)-6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-indazole-3-carboxylate,
ethyl 6-(-)-6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-indazole-3-carboxylate,
ethyl 6-(+)-6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-indazole-3-carboxylate,

ethyl 6,6-bis(4-fluorophenyl)-6,7-dihydro-1H-indazole-3-carboxylate,
and
ethyl 7-methyl-6,6-diphenyl-6,7-dihydro-1H-indazole-3-carboxylate.

5 7. The compound according to claim 4 wherein R_2 is CORa_4 and Ra_4 is Ar
or $(\text{C}_3\text{-C}_5)\text{cycloalkyl}$.

8. The compound according to claim 7 selected from the group consisting
of:

10 cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone,
cyclobutyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone,
(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)phenylmethanone,
(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)-(1H-pyrrol-3-yl)methanone,
6-(R,S)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-indazol-
15 3-yl]methanone,
(-)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-indazol-3-
yl]methanone,
(+)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-indazol-3-
yl]methanone, and
20 cyclopropyl[6,6-bis(4-fluorophenyl)-6,7-dihydro-1H-indazol-3-
yl]methanone.

9. The compound according to claim 4 wherein R_2 is C(O)-NHRa_2 , $\text{C(O)-N(Ra}_3\text{)-ORa}_3$ or $\text{C(O)-N(Ra}_2')$.

25 10. The compound according to claim 9 selected from the group consisting
of:

30 N-(cyclopropyl)-6,6-diphenyl-6,7-dihydro-1H-indazole-3-carboxamide,
azetidin-1-yl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone,
(N-methoxy-N-methyl)-6,6-diphenyl-6,7-dihydro-1H-indazole-3-
carboxamide, and
aziridin-1-yl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone.

11. The compound according to claim 4 wherein R_2 is $C(R_{a4})=N-R_b$.

12. The compound according to claim 11 selected from the group consisting

of:

- 5 (E,Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl) methanone
oxime,
(E)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl) methanone
oxime,
(Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl) methanone
10 oxime,
(E,Z)cyclobutyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
oxime,
(E)cyclobutyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
oxime,
15 (Z)cyclobutyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
oxime,
(E,Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-2H-indazol-3-yl)methanone
O-methyloxime,
(E)cyclopropyl(6,6-diphenyl-6,7-dihydro-2H-indazol-3-yl)methanone
20 O-methyloxime,
(Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-2H-indazol-3-yl)methanone
O-methyloxime,
(E,Z)6,6-diphenyl-6,6-dihydro-1H-indazole-3-carbaldehyde O-
methyloxime,
25 (E, Z)cyclobutyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone O-
allyloxime,
(E)cyclobutyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone O-
allyloxime,
(Z)cyclobutyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone O-
30 allyloxime,
(E,Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-allyloxime,

(Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-allyloxime,
(E)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-allyloxime,
5 (E,Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-(2-methoxyethyl)oxime,
(Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone O-
(2-methoxyethyl)oxime,
(E)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone O-
10 (2-methoxyethyl)oxime,
(E,Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-benzyloxime,
(Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-benzyloxime,
15 (E)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-benzyloxime,
(E,Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-(4-nitrobenzyl)oxime,
(Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
20 O-(4-nitrobenzyl)oxime,
(E)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-(4-nitrobenzyl)oxime,
(E,Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-(2-dimethylaminoethyl)oxime,
25 (Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-(2-dimethylaminoethyl)oxime,
(E)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-(2-dimethylaminoethyl)oxime,
(E,Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
30 O-(2-fluoroethyl)oxime,
(Z)cyclopropyl(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)methanone
O-(2-fluoroethyl)oxime,

(E)cyclopropyl[6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl]methanone
O-(2-fluoroethyl)oxime,
(E,Z)-6-(R,S)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-
indazol-3-yl]methanone oxime,
5 (E)-6-(R,S)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-
indazol-3-yl]methanone oxime,
(Z)-6-(R,S)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-
indazol-3-yl]methanone oxime,
(-)-6-(Z)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-
10 indazol-3-yl]methanone oxime,
(-)-6-(E)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-
indazol-3-yl]methanone oxime,
(+)-6-(Z)-cyclopropyl[6-(4-fluorophenyl)-6-phenyl-6,7-dihydro-1H-
indazol-3-yl]methanone oxime,
15 (E,Z)cyclopropyl[6,6-bis(4-fluorophenyl)-6,7-dihydro-1H-indazol-3-
yl]methanone oxime,
(Z)cyclopropyl[6,6-bis(4-fluorophenyl)-6,7-dihydro-1H-indazol-3-
yl]methanone oxime, and
(E)cyclopropyl[6,6-bis(4-fluorophenyl)-6,7-dihydro-1H-indazol-3-
20 yl]methanone oxime.

13. The compound according to claim 4 wherein R_2 is $NH-C(O)Ra_4$.

14. The compound according to claim 13 selected from the group consisting

25 of:

N-(6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl)cyclopropylamide, and
N-[6,6-diphenyl-6,7-dihydro-1H-indazol-3-yl]benzamide

15. The compound according to claim 4 wherein R_2 is Ar.

16. The compound according to claim 15 selected from the group consisting

30 of:

3-(3-methyl[1,2,4]oxadiazol-5-yl)-6,6-diphenyl-6,7-dihydro-1H-indazole,

3,6,6-triphenyl-6,7-dihydro-1H-indazole,
6,6-diphenyl-3-pyrid-3-yl-6,7-dihydro-1H-indazole, and
6,6-diphenyl-3-thiophen-3-yl-6,7-dihydro-1H-indazole.

5 17. The compound according to claim 4 wherein R_2 is CN.

18. The compound according to claim 14 wherein the compound is 6,6-diphenyl-6,7-dihydro-1H-indazole-3-carbonitrile.

10 19. The compound according to claim 1 wherein Z is SO_2R_3 or COR_3 .

20. The compound according to claim 19 selected from the group consisting
of:

6,6-diphenyl-1-(4-toluenesulphonyl)-6,7-dihydro-1H-indazol-3-ylamine

15 and

1-(3-Amino-6,6-diphenyl-6,7-dihydroindazol-1-yl)propenone.

21. The compound according to claim 1 wherein Z is 4-aminophenyl.

20 22. The compound according to claim 21 wherein the compound is ethyl
1-(4-aminophenyl)-6,6-diphenyl-1H-indazole-3-carboxylate.

23. The compound according to claim 1 wherein X is CH, Y is N and R_2 is
 $C(O)-OR_{a1}$.

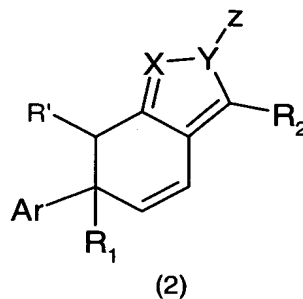
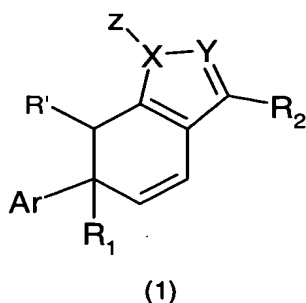
25 24. The compound according to claim 23 wherein the compound is ethyl
5,5-diphenyl-4,5-dihydro-2H-isoindole-1-carboxylate.

25. The compound according to claim 1 wherein X is N, Y is CH and R_2 is
30 $C(O)-OR_{a1}$.

26. The compound according to claim 25 wherein the compound is ethyl
6,6-diphenyl-6,7-dihydro-1H-indole-3-carboxylate.

27. A method for the treatment of tumors comprising administering to a patient in need of said treatment a therapeutically effective amount of a compound of formula (1) or formula (2)

5



wherein:

X and Y independently are N or CH wherein at least one of X and Y is N;

Ar is:

10 phenyl optionally substituted with one or more substituents selected from the group consisting of: halogen, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, thio(C₁-C₄)alkyl, NO₂, NH(C₁-C₄)alkyl and N((C₁-C₄)alkyl)₂ wherein said alkyl may optionally form a 4 to 6 membered ring together with the heteroatom to which it is attached and an ortho carbon of the phenyl
15 wherein said 4 to 6 membered ring may contain a second hetero atom selected from the group consisting of O, S and N, or

5 or 6 membered aromatic heterocycle containing one or two hetero atoms selected from the group consisting of O, N and S, and optionally substituted with one or more halogen, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, thio(C₁-C₄)alkyl, NH(C₁-C₄)alkyl, N((C₁-C₄)alkyl)₂ wherein said alkyl may
20 optionally form a 4 to 6 membered ring together with the heteroatom to which it is attached and an ortho carbon of said heterocycle wherein said 4 to 6 membered ring may optionally contain a second hetero atom selected from the group consisting of O, S and N,

25 Z is H, 4-aminophenyl, SO₂R₃ or COR₃ wherein R₃ is (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl, Ar as defined above, (C₂-C₆)alkenyl or (C₂-C₆)alkynyl;

R₁ is H, (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl or Ar as defined above;

R' is H or (C₁-C₄)alkyl; and

when Z is H, R_2 is selected from the group consisting of:

cyano,

$C(O)-ORa_1$ wherein Ra_1 is methyl, ethyl or isopropyl,

$C(O)-NHRa_2$ wherein Ra_2 is cyclopropyl,

$C(O)-N(Ra_2')$, wherein $N(Ra_2')$ is aziridinyl or azetidiny, optionally substituted with (C_1-C_4) alkyl or Ar as defined above,

$C(O)-N(Ra_3)-ORa_3$ wherein each Ra_3 may be identical or different and each Ra_3 is independently selected from the group consisting of methyl, ethyl or cyclopropyl,

$C(O)Ra_4$ wherein Ra_4 is Ar as defined above or (C_3-C_5) cycloalkyl optionally substituted with (C_1-C_4) alkyl or Ar as defined above,

$C(Ra_4)=N-Rb$ wherein:

Ra_4 is H, Ar as defined above, or (C_3-C_5) cycloalkyl optionally substituted with (C_1-C_4) alkyl or Ar as defined above, and

Rb is (C_1-C_2) alkyl, (C_3-C_5) cycloalkyl, hydroxyl, (C_1-C_4) alkoxy, (C_2-C_4) alkenyloxy, or (C_1-C_4) alkylenoxy wherein said (C_1-C_4) alkylenoxy optionally may be substituted with halogen or a group selected from the group consisting of carboxyl, $(CH_2)_nAr$ wherein n is 0 or 1 and Ar is as defined above, (C_1-C_4) alkoxy, NH_2 , $NH(C_1-C_4)$ alkyl, and $N((C_1-C_4)alkyl)_2$ wherein said alkyls together with the heteroatom to which they are attached may optionally form a 3 to 6 membered ring which may optionally contain a second hetero atom selected from the group consisting of O, S and N,

$NH-C(O)Ra_4$ wherein Ra_4 is H, Ar as defined above, or (C_3-C_5) cycloalkyl optionally substituted with (C_1-C_4) alkyl or Ar as defined above,

$NHRa_4$ wherein Ra_4 is H, Ar as defined above, or (C_3-C_5) cycloalkyl optionally substituted with (C_1-C_4) alkyl or Ar as defined above,

phenyl, and

5 to 6 membered aromatic heterocycle containing 1 to 3 hetero atoms selected from the group consisting of O, N and S; and

when Z is SO_2R_3 or COR_3 , R_2 is carboxyl, NH_2 , $NH(C_1-C_4)alkyl$, $N((C_1-C_4)alkyl)_2$ or (C_3-C_5) cycloalkylamino; or

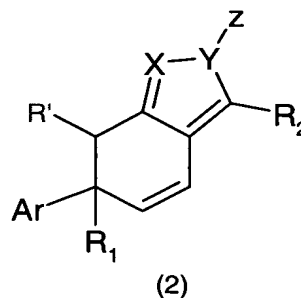
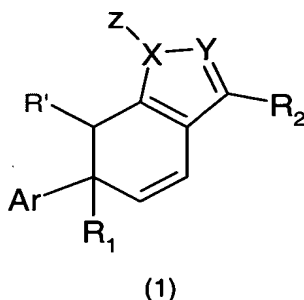
a stereoisomeric form of the compound of formula (1) or formula (2), or mixtures of the stereoisomeric forms thereof in any ratio; or
a pharmaceutically acceptable salt of the compound of formula (1) or formula (2).

28. The method of claim 27 wherein the therapeutically effective amount comprises an amount sufficient to inhibit microtubule polymerization.

29. The method of claim 27 wherein the therapeutically effective amount comprises a therapeutically effective endothelial cell detaching amount.

30. The method of claim 27 wherein the therapeutically effective amount comprises an amount sufficient to inhibit vascularization of said tumors.

31. A method for the treatment of cancerous cells comprising administering to a patient in need of said treatment a therapeutically effective amount of a compound of formula (1) or formula (2)



wherein:

X and Y independently are N or CH wherein at least one of X and Y is N;

Ar is:

phenyl optionally substituted with one or more substituents selected from the group consisting of: halogen, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, thio(C₁-C₄)alkyl, NO₂, NH(C₁-C₄)alkyl and N((C₁-C₄)alkyl)₂ wherein said alkyl may optionally form a 4 to 6 membered ring together with the heteroatom to which it is attached and an ortho carbon of the phenyl wherein said 4 to 6 membered ring may contain a second hetero atom selected from the group consisting of O, S and N, or

5 or 6 membered aromatic heterocycle containing one or two hetero atoms selected from the group consisting of O, N and S, and optionally substituted with one or more halogen, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, thio(C₁-C₄)alkyl, NH(C₁-C₄)alkyl, N((C₁-C₄)alkyl)₂ wherein said alkyl may optionally form a 4 to 6 membered ring together with the heteroatom to which it is attached and an ortho carbon of said heterocycle wherein said 4 to 6 membered ring may optionally contain a second hetero atom selected from the group consisting of O, S and N,

Z is H, 4-aminophenyl, SO₂R₃ or COR₃ wherein R₃ is (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl,

Ar as defined above, (C₂-C₆)alkenyl or (C₂-C₆)alkynyl;

R₁ is H, (C₁-C₄)alkyl, (C₃-C₆)cycloalkyl or Ar as defined above;

R' is H or (C₁-C₄)alkyl; and

when Z is H, R₂ is a selected from the group consisting of:

cyano,

C(O)-ORa₁ wherein Ra₁ is methyl, ethyl or isopropyl,

C(O)-NHRa₂ wherein Ra₂ is cyclopropyl,

C(O)-N(Ra₂'), wherein N(Ra₂') is aziridinyl or azetidyl, optionally substituted with (C₁-C₄)alkyl or Ar as defined above,

C(O)-N(Ra₃)-ORa₃ wherein each Ra₃ may be identical or different and each Ra₃ is independently selected from the group consisting of methyl, ethyl or cyclopropyl,

C(O)Ra₄ wherein Ra₄ is Ar as defined above or (C₃-C₅)cycloalkyl optionally substituted with (C₁-C₄)alkyl or Ar as defined above,

C(Ra₄)=N-Rb wherein:

Ra₄ is H, Ar as defined above, or (C₃-C₅)cycloalkyl optionally substituted with (C₁-C₄)alkyl or Ar as defined above, and

Rb is (C₁-C₂)alkyl, (C₃-C₅)cycloalkyl, hydroxyl, (C₁-C₄)alkoxy, (C₂-C₄)alkenyloxy, or (C₁-C₄)alkylenoxy wherein said (C₁-C₄)alkylenoxy optionally may be substituted with halogen or a group selected from the group consisting of carboxyl, (CH₂)_nAr wherein n is 0 or 1 and Ar is as defined above, (C₁-C₄)alkoxy, NH₂, NH(C₁-C₄)alkyl, and N((C₁-C₄)alkyl)₂ wherein said alkyls together with the heteroatom to which they are attached may optionally form

a 3 to 6 membered ring which may optionally contain a second hetero atom selected from the group consisting of O, S and N, NH-C(O)Ra₄ wherein Ra₄ is H, Ar as defined above, or (C₃-C₅)cycloalkyl optionally substituted with (C₁-C₄)alkyl or Ar as defined above, 5 NH-Ra₄ wherein Ra₄ is H, Ar as defined above, or (C₃-C₅)cycloalkyl optionally substituted with (C₁-C₄)alkyl or Ar as defined above, phenyl, and

5 to 6 membered aromatic heterocycle containing 1 to 3 hetero atoms selected from the group consisting of O, N and S; and

10 when Z is SO₂R₃ or COR₃, R₂ is carboxyl, NH₂, NH(C₁-C₄)alkyl, N((C₁-C₄)alkyl)₂ or (C₃-C₅)cycloalkylamino; or
a stereoisomeric form of the compound of formula (1) or formula (2), or mixtures of the stereoisomeric forms thereof in any ratio; or
a pharmaceutically acceptable salt of the compound of formula (1) or formula (2).

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32. The method of claim 31 wherein the therapeutically effective amount comprises an amount sufficient to inhibit microtubule polymerization.

33. The method of claim 31 wherein the therapeutically effective amount 20 comprises a therapeutically effective endothelial cell detaching amount.

34. The method of claim 31 wherein the therapeutically effective amount comprises an amount sufficient to inhibit vascularization of said cancerous cells.

25 35. A pharmaceutical composition comprising one or more compounds of formula (1) or formula (2) according to claim 1 and one or more pharmaceutically acceptable carriers, diluents, adjuvants or excipients.